

(FILE 'USPAT' ENTERED AT 09:56:29 ON 30 OCT 1997)

L1 2497 S TUMOR NECROSIS FACTOR OR TNF
L2 22 S L1 (10A) BINDING PROTEIN
L3 12 S L2 AND SOLUBLE

=> d 1-

1. 5,660,826, Aug. 26, 1997, Therapeutic sepsis treatment using antagonists to PTHrP; Carl Grunfield, et al., 424/145.1, 158.1; 514/885 :IMAGE AVAILABLE:
2. 5,656,272, Aug. 12, 1997, Methods of treating TNF-.alpha.-mediated Crohn's disease using chimeric anti-TNF antibodies; Junming Le, et al., 424/133.1, 139.1, 145.1; 435/69.1, 69.6, 69.7; 530/387.3, 388.23 :IMAGE AVAILABLE:
3. 5,641,647, Jun. 24, 1997, Serum free medium; Dina Fischer, et al., 435/69.1, 395, 406 :IMAGE AVAILABLE:
4. 5,633,145, May 27, 1997, **TNF.alpha. receptor-derived binding protein**; Marc Feldmann, et al., 435/69.1, 69.7, 252.3, 320.1; 536/23.4, 23.5 :IMAGE AVAILABLE:
5. 5,624,826, Apr. 29, 1997, Cloning vector plasmid vector-primer derived therefrom and preparation method of the same; Seishi Kato, et al., 435/91.4, 172.3, 320.1; 935/18, 22 :IMAGE AVAILABLE:
6. 5,610,279, Mar. 11, 1997, Human TNF receptor; Manfred Brockhaus, et al., 530/387.3; 435/69.5 :IMAGE AVAILABLE:
7. 5,606,031, Feb. 25, 1997, Production and purification of biologically active recombinant neurotrophic protein in bacteria; Jack Lile, et al., 530/416, 402, 408, 417 :IMAGE AVAILABLE:
8. 5,606,023, Feb. 25, 1997, Mutant tumor necrosis factor proteins; Mann-Jy Chen, et al., 530/351; 424/85.2; 435/69.52 :IMAGE AVAILABLE:
9. 5,605,690, Feb. 25, 1997, Methods of lowering active TNF-.alpha. levels in mammals using tumor necrosis factor receptor; Cindy A. Jacobs, et al., 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868 :IMAGE AVAILABLE:
10. 5,582,998, Dec. 10, 1996, Monoclonal antibodies against human **TNF-binding protein I (TNF-BP I)** and immunoassays therefor; G unther Adolf, 435/7.1, 7.92, 7.94, 70.21, 334; 436/811, 815; 530/388.1 :IMAGE AVAILABLE:
11. 5,512,544, Apr. 30, 1996, Pharmaceutical compositions comprising an anticytokine; David Wallach, et al., 514/12, 21; 530/350 :IMAGE AVAILABLE:
12. 5,478,925, Dec. 26, 1995, Multimers of the soluble forms of TNF receptors, their preparation and pharmaceutical compositions containing them; David Wallach, et al., 530/351; 424/85.1, 158.1, 450 :IMAGE AVAILABLE:
13. 5,470,829, Nov. 28, 1995, Pharmaceutical preparation; Per Prisell, et al., 514/12; 424/85.1; 514/2, 8, 21; 525/54.1 :IMAGE AVAILABLE:
14. 5,464,820, Nov. 7, 1995, Specific inhibitors of tissue kallikrein; James Burton, et al., 514/16, 17, 18; 530/329, 331 :IMAGE AVAILABLE:
15. 5,426,181, Jun. 20, 1995, DNA encoding cytokine-induced protein,

16. 5,395,760, Mar. 7, 1995, DNA encoding tumor necrosis factor-.alpha. and -.beta. receptors; Craig A. Smith, et al., 435/365; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 :IMAGE AVAILABLE:
17. 5,359,039, Oct. 25, 1994, Isolated poxvirus A53R-equivalent tumor necrosis factor antagonists; Craig A. Smith, et al., 530/350; 424/186.1, 232.1; 530/826; 536/23.72; 930/220 :IMAGE AVAILABLE:
18. 5,359,037, Oct. 25, 1994, Antibodies to **TNF binding protein I**; David Wallach, et al., 530/388.22; 424/143.1, 172.1; 530/388.1, 389.1 :IMAGE AVAILABLE:
19. 5,344,915, Sep. 6, 1994, Proteins and the preparation thereof; Hans-Georg LeMaire, et al., 530/350, 395, 413, 416 :IMAGE AVAILABLE:
20. 5,288,852, Feb. 22, 1994, Human tumor necrosis factor polypeptides; Massaki Yamada, et al., 530/351; 424/85.1; 435/69.5, 69.7; 530/395; 930/144 :IMAGE AVAILABLE:
21. 5,147,638, Sep. 15, 1992, Inhibition of tumor growth by blockade of the protein C system; Charles T. Esmon, et al., 424/85.1, 85.2, 85.4, 85.5, 152.1, 172.1, 282.1; 435/212; 514/2, 8, 12; 530/351, 381, 388.25, 389.3 :IMAGE AVAILABLE:
22. 5,136,021, Aug. 4, 1992, TNF-inhibitory protein and a method of production; Wlodzimierez E. Dembinski, et al., 530/350, 351, 369 :IMAGE AVAILABLE:

=> d 4 bib date ab

US PAT NO: 5,633,145 :IMAGE AVAILABLE: L2: 4 of 22
DATE ISSUED: May 27, 1997
TITLE: **TNF.alpha. receptor-derived binding protein**
INVENTOR: Marc Feldmann, Hammersmith, United Kingdom
Patrick W. Gray, Bothell, WA
Martin J. C. Turner, Ann Arbor, MI
Fionula M. Brennan, Hammersmith, United Kingdom
ASSIGNEE: The Mathilda and Terence Kennedy Institute of Rheumatology
, London, England (foreign corp.)
APPL-NO: 08/050,319
DATE FILED: May 10, 1993
ART-UNIT: 182
PRIM-EXMR: John Ulm
LEGAL-REP: Reed & Robins

L2: 4 of 22
TITLE: **TNF.alpha. receptor-derived binding protein**
US PAT NO: 5,633,145 DATE ISSUED: May 27, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/050,319 DATE FILED: May 10, 1993
FRN-PR. NO: 9022648 FRN FILED: Oct. 18, 1990
FRN-PR. CO: United Kingdom
PCT-NO: PCT/GB91/01826 PCT-FILED: Oct. 18, 1991
371-DATE: May 10, 1993
102(E)-DATE: May 10, 1993
PCT-PUB-NO: WO92/07076 PCT-PUB-DATE: Apr. 30, 1992

ABSTRACT:

A polypeptide is provided which is capable of binding human TNF.alpha. and which has the first three cysteine-rich subdomains, but not the fourth cysteine-rich subdomain, of the extracellular binding domain of a receptor selected from the group consisting of the 55 kD and 75 kD receptors for human TNF.alpha.. The ability of the polypeptide to bind TNF.alpha. means that it can be used for treating diseases mediated by TNF.alpha. activity, such as rheumatoid arthritis.